PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

	Date of mailing *(day/month/year)*
Applicant's or agent's file reference FP05-0112-00	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2005/005247	23.03.2005	26.03.2004

International Patent Classification (IPC) or both national classification and IPC

Applicant
HISAMITSU PHARMACEUTICAL CO., INC.

1. This opinion contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP Facsimile No.	Authorized officer Telephone No.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2005/005247

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☒ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☒ in computer readable form

   c. time of filing/furnishing

      ☐ contained in the international application as filed.

      ☒ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2005/005247

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:

   ☐ paid additional fees

   ☐ paid additional fees under protest

   ☒ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

The common matter of claims 1-10 appears to be "controlling p73 apoptosis induction activity by means a protein that acts on p73".

However the search discovered documents (Nature, 1999, Vol. 399, J. G. GONG et al., pp. 806-809, R. AGAMI et al., pp. 809-813 and Z. M. YUAN et al., pp. 814-817) disclosing that "tyrosine kinase c-Abl controls p73 apoptosis induction activity by binding to p73 or phosphorylating p73", so this common matter is obviously not novel.

Thus, "controlling p73 apoptosis induction activity by means of a protein that acts on p73" falls within the scope of prior art, and this common matter cannot be called a special technical feature.

Therefore, the inventions of the claims are classified according to the general inventive concept of "controlling p73 apoptosis induction activity by means of IKK-alpha" and the general inventive concept of "controlling p73 apoptosis induction activity by means of UFD2a (SEQ ID NO:26)".

Consequently, the claims describe 2 general inventive concepts involving "controlling p73 apoptosis induction activity by means of a protein that acts on p73," but because these two general inventive concepts do not share a novel special technical feature, this international application does not comply with the requirement of unity of invention in accordance with Enforcement Rule 13 (PCT Rules 13.1, 13.2 and 13.3).

4. Consequently, this opinion has been established in respect of the following parts of the international application:

   ☐ all parts

   ☒ the parts relating to claims Nos. 1-8

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2005/005247

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-8	YES
	Claims		NO
Inventive step (IS)	Claims	1-4	YES
	Claims	5-8	NO
Industrial applicability (IA)	Claims	1-8	YES
	Claims		NO

2. Citations and explanations:

Document 1: Y. HU et al., Science, 1999, Vol. 284, pp. 316-320
Document 2: C. H. REGNIER et al., Cell, 1997, Vol. 90, pp. 373-383
Document 3: R. K. SRIVASTAVA, Proc. Natl. Acad. Sci., 1999, Vol. 96, pp. 3775-3780

Document 1 describes a knockout mouse lacking the mouse IkappaB kinase alpha (IKK alpha gene), and describes that this knockout mouse has a developmental digiti manus formation defect, and that this defect occurs due to a lack of cell apoptosis in the region that forms the digiti manus (see in particular Fig. 3).

Document 2 describes human IKK alpha corresponding to mouse CHUK (hereunder, IKK alpha), along with the amino acid sequence of this human IKK alpha, and mutant IKK alpha K44A lacking kinase activity obtained by substituting alanine for the #44 lysine of this amino acid sequence.

The inventions described in claims 5 and 6 do not appear to involve an inventive step over documents 1 and 2.

It is obvious to a person skilled in the art from document 1 that mouse IKK alpha functions to promote apoptosis, and human IKK alpha having high homolog with the mouse amino acid sequence is well-known as described in document 2.

Therefore, it would be easy for a person skilled in the art to use the human IKK described in document 2 which has high homology with the mouse amino acid sequence to promote apoptosis based on document 1.

The inventions described in claims 7 and 8 do not appear to involve an inventive step over documents 1, 2 and 3.

Using a mutant lacking the kinase activity or other function of a protein having a kinase activity or other function as a dominant negative mutant to impede signalling is a well-known matter as described for example in document 3.

Consequently, it would be easy for a person skilled in the art to use the mutant IKK alpha K44A described in document 2 as a dominant negative mutant that impedes apoptosis signalling in order to control apoptosis based on document 1.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2005/005247

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V

The inventions described in claims 1-4 are not described in any of the documents cited in the ISR, nor would they be obvious to a person skilled in the art based on the descriptions of those documents.